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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,826	07/10/2006	Markus Linder	0365-0662PUS1	5038

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EXAMINER
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MOHAMED, ABDEL A

ART UNIT	PAPER NUMBER
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1654

NOTIFICATION DATE	DELIVERY MODE
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03/20/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/563,826	<b>Applicant(s)</b> LINDER ET AL.	
	<b>Examiner</b> Abdel A. Mohamed	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 05 December 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) 3 and 4 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2, 6 and 7 is/are rejected.
- 7) ☐ Claim(s) 1-11 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 July 2006 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>See Continuation Sheet</u> .                                  | 6) <input type="checkbox"/> Other: _____                          |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :1/6/06; 4/12/06; 4/25/06 and 6/29/06.

### **DETAILED ACTION**

#### **ACKNOWLEDGMENT TO PRIORITY, PRELIMINARY AMENDMENT, IDS, RESPONSE TO SEQUENCE ELECTION REQUIREMENT, STATUS OF THE APPLICATION AND CLAIMS**

1. This application is filed under 35 U.S.C. 371 on 07/10/06 having a filing date of 07/08/04 of PCT/FI04/00439. Acknowledgement is made of Applicant's claim for priority based on Finland Application No. 20031050 having a filing date of 07/09/03. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119, which papers have been placed of record in the file. The preliminary amendment filed 01/06/06 and the information disclosure statement (IDS) and Form PTO-1449 filed 01/06/06, 04/12/06, 04/15/06 and 06/29/06, respectively and the response for sequence election filed 12/05/08 are acknowledged, entered and considered. In view of Applicant's request claims 4-11 have been amended. Claims 1-11 are now pending in the application.

#### **ELECTION WITH TRAVERSE**

2. Applicant's election with traverse of SEQ ID NO:30 of claim 5 in the communication filed 12/05/08 is acknowledged. The traversal is on the ground(s) that **Claim 5 is directed to the elected species. As acknowledged by the Examiner, at least claims 1-4 and 6-11 are generic.** According to MPEP 803, if the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to independent or distinct inventions is unpersuasive. However, with respect to Applicant's arguments that the SEQ ID NO:28 (His<sub>4</sub>) is part of SEQ ID

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NOS:29 and 30, also, His<sub>2</sub> is part of SEQ ID NOS:28, 29 and 30 (i.e., wherein X<sub>1</sub> is His or X<sub>1</sub>, X<sub>1</sub> or repeats thereof or two or more repeat of X<sub>1</sub>) is persuasive and will be examined with the elected sequence (SEQ ID NO:30). Thus, sequence SEQ ID NOS:28-30 including all the limitations of claim 1 as long as it reads on X<sub>1</sub>, X<sub>1</sub> or repeat thereof will be examined with the elected SEQ ID NO:30 (i.e., claim 1 to the extent as it reads only on His which is X<sub>1</sub> or X<sub>1</sub>, X<sub>1</sub> or repeats thereof, claim 2, claim 5 excluding SEQ ID NO:9 and claims 6-11 will be examined as elected invention.

In regard to Applicant's allegation that **as acknowledged by the Examiner, at least claims 1-4 and 6-11 are generic to species of claim 5** is not persuasive. Contrary to Applicant's allegation, the election is **not** an election of species and as stated in the previous Office action the sequences are patentably distinct because they are unrelated sequences and each unrelated sequence is considered a separate and distinct product, therefore, a further restriction is applied to each sequences, particularly, to SEQ ID NO:9 as acknowledged by Applicant. Further, there is no sequence linking each other, it is only consensus. For an elected invention drawn to either amino acid or polypeptide sequences, the Applicant must further elect a **single** amino acid or a **single** polypeptide sequence (See MPEP 803.04). In the instant case, which ever sequence Applicant elects in claim 5, claims 1-4 and 6-11 will be examined along the elected sequence. Due to the increasingly large size of sequence databases which must be searched and the increasing numbers of applications requiring sequence searches, it creates an undue burden on the Office to search more than a single sequence (product) per application. For these reasons, the requirements of 37 CFR 1.141 *et seq.* are no longer waived and Applicant is required to elect a **single** sequence for examination. Applicant is reminded that this is a

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**restriction requirement, not an election of species.** Therefore, the **sequence election requirement is a restriction requirement, not an election of species** as alleged by Applicant.

Thus, they are unrelated and are different inventions having independent and distinct formulations, which are not connected in design, operation or effect.

It is noted that SEQ ID NOS:28-30 will be examined together as long as they are directed to  $X_1$  or  $X_1$ ,  $X_1$  or repeats thereof wherein  $X_1$  is His. Therefore, sequences recited in claim 5 other than SEQ ID NO:9, claims 3 and 4 are withdrawn as non-elected invention and sequence for the reasons of record. Hence, the Office action is directed to the merits of claims 1 and 5 as to the extent it reads on  $X_1$  which is His and claims dependent thereof (claims 2 and 6-11) as *per* elected invention and sequences and Applicant is advised to cancel non-elected inventions of claim 1 which comprises  $Y_n$  which is any amino acid and SEQ ID NO:9 of claim 5 is directed  $X_1$  is His and  $Y_n$  is any amino acid as well as claims 3 and 4 having the limitation of  $Y_n$  in the next communication.

The requirement is still deemed proper and is therefore made FINAL.

### **OBJECTION TO THE CLAIMS**

3. Claims 1-11 are objected to for being drawn to non-elected subject matter.

Claims 5-7 are objected in the recitation "...selected from the group...." because it is not clear if Applicant intends a Markush format. If Applicant intends to use a Markush format, then, the Office recommends to use of the phrase ".....selected from the group consisting of....." in listing species to ensure the Markush group is "closed".

Claims 6-8 are objected in the recitation “a ion”. It is believed typographical error.  
Amendment of the claims to recite “an ion” would obviate this objection.

### **CLAIMS REJECTION-35 U.S.C. § 112<sup>2nd</sup> PARAGRAPH**

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 2, 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite in depending on itself and has not been considered further on the merits. Appropriate correction is required.

Claims 2, 6 and 7 are indefinite in the recitation “preferably” because the phrase makes the choice “optional”. If an ingredient, a step, or other structural element is truly optional (e.g., preferentially this amino acids or that, or preferably this metal or that) i.e., its presence is not necessary for attainment of the result that is an object of the invention, then recitation thereof does not belong in the claims.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim

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indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 2 recites the broad recitation of a length of amino acids ranging from 2 to 10 and the claim also recites a length ranging from 4 to 8 amino acids which is the narrower statement of the range/limitation. ). In the present instance, claims 6 and 7 recite the broad range of metal limitations and a narrow range of metal limitations.

#### **CITATION OF RELEVANT PRIOR ART**

5. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Hartley (U.S. Patent No. 5,449,758) discloses a protein size marker ladder comprising a collection of protein fragments obtained by the partial cleavage of one or more multidomain proteins (e.g., SEQ ID NO:6 which is His<sub>6</sub>) by one or more cleaving agents.

Stahl et al (U.S. Patent No. 5,470,952) teach the tagging of chimeric protein by His<sub>6</sub> (SEQ ID NO:1) to allow rapid purification by meal-chelate chromatography.

Ballinger et al (U.S. Patent No. 5,780,285) disclose His<sub>6</sub> (SEQ ID NO:51) that binds metal affinity column.

Bolen et al (U.S. Patent No. 6,844,178 B2) disclose a fusion polypeptide called polyHis-enterokinase having the amino acid sequence in (SEQ ID NO:6) comprising from 1-10 His amino acids.



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Zhang et al (U.S. Patent No. 7,179,784 B2) describe dipolar oligopeptides such as (SEQ ID NO:53) His<sub>10</sub> that can self-assemble to form regular structures.

Shyh-Horng Chiou (J. Biochem., Vol. 94, pages 1259-1267, 1983) examines the various transition metal ions and reducing agents under comparable conditions to determine the basic requirements for both DNA degradation and protein scission activities by using the tripeptide diglycyl-L-histidine, wherein ascorbic acid is the most effective reducing agent to achieve the cleavage of DNA and the protein in presence of copper ions.

Dou et al (Prep. Biochem. & Biotechnol., Vol. 30, No. 1, pages 69-78, 2000) disclose the use of palladium(II) complex as cleavage agent for the production of peptide drugs from gene-engineering protein by introducing a codon of Cys-His units.

However, none of the prior art of record either singularly or in combination teach or suggest employing a method for cleaving a protein or a peptide at specific site by contacting at a predetermined cleavage site of the protein or peptide wherein the amino acid sequence comprises **X<sub>1</sub>X<sub>1</sub>, or repeats thereof or two or more repeats of X<sub>1</sub>Y<sub>n</sub>, wherein N= 1, X<sub>1</sub> is His.**

Therefore, there is no indication in any of the prior art cited above or in the prior art documents of using pairs of histidine (His-His) or repeats of pairs thereof in which histidine is the first amino acid and constructed at a predetermined cleavage site and the protein or peptide is allowed to react with free metal ions in a buffer in the manner claimed in claims 1, 2, and 5-11 of the instant invention.

#### CONCLUSION AND FUTURE CORRESPONDANCE

6. No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272-0955.

The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mohamed/A. A. M./  
Examiner, Art Unit 1654

/JON P WEBER/  
Supervisory Patent Examiner, Art Unit 1657